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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,780	08/30/2001	Kevin P. Baker	P2548P1C10	2570

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EXAMINER	
HELMS, LARRY RONALD	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,780	BAKER ET AL.	
	Examin r	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication app ars on the cover sh et with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 22-26 have been amended.

Claims 35-36 have been added.

2. Claims 22-36 are pending and under examination.

3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

4. The following Office Action contains some NEW GROUNDS of rejection.

Claim Objections

5. Claim 35 is objected to because of the following informalities: Claim 35 contains a typographical error in the term "avid" in line two, the term should be "acid". Appropriate correction is required.

Rejections Withdrawn

6. The rejection of claims 22-27, 30-31, 33-34 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of arguments.

7. The rejection of claims 22-27, 32-34 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in view of the successful completion of the deposit requirements.

Response to Arguments

8. The rejection of claims 22-36 under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility is maintained.

The response filed 11/6/03 has been carefully considured but is deemed not to be persuasive. The response states that Example 28, the gene amplification experiment demonstrates that the nucleic acid encoding PRO357 is amplified in lung and colon tumors and this supports a diagnostic utility for nucleic acids, polypeptides and antibodies to PRO 357 (see page 9-11 of response). In response to this argument, only SEQ IS NO:68 is demonstrated to be amplified in lung and colon tumor. No other nucleic acids are amplified or taught to be amplified in lung or colon tumor. The response then states that the Goddard declaration states that at least a 2-fold increase in gene copy number in a tumor tissue sample relative to normal is significant and serves as a diagnostic marker for absence or presence of tumor (see page 10 of response). In response to this argument, the declaration of Dr. Goddard has been carefully considured but is deemed not to be persuasive. While the increase in copy number is seen for SEQ ID NO:68, there is no other nucleic acid or any other nucleic acid that encodes SEQ ID NO:69 or is at least 80% identical to a polypeptide of SEQ ID

NO:69 that is demonstrated to be differentially expressed in lung or colon cancerous tissue. The response states that the second declaration of Dr. Ashkenazi explains that if over-expression of the gene product does not parallel gene amplification in certain tumor types but does so in others, then parallel monitoring of gene amplification and gene product over-expression enables more accurate tumor classification and hence better determination of suitable therapy (see page 12). In response to this argument, the declaration of Dr. Ashkenazi has been carefully considured but is deemed not to be persuasive. Again the declaration does not provide any evidence that the protein would be expressed. The declaration only states that combining gene amplification and gene product monitoring would be better for therapy. There is no evidence of record that any other nucleic acid other that SEQ ID NO:68 is amplified in colon or lung tumor and as such there would be no specific utility for any nucleic acid encoding a polypeptide that is at least 80% identical to SEQ ID NO:69 or any nucleic acid other than SEQ ID NO:68 which encodes SEQ ID NO:69.

Thus, one skill in the art would conclude that absence evidence that the polypeptide is expressed at an elevated level one would conclude that claimed invention is not supported by either a substantial asserted utility or a well established utility.

9. The rejection of claims 22-36 rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention is maintained.

The response filed 11/6/03 has been carefully considured and is deemed not to be persuasive. The response states that the remarks above address the 101 rejection and because of this rejection should be withdrawn. In response to this argument, the remarks above address the rejection of 101 and as such one would not know how to use the claimed invention.

10. Claims 22-26, 33-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed 11/06/03 has been carefully considured but is deemed not to be persuasive. The response states that several features such as the open reading frame, translation initiation and the precursors of PRO 357 are disclosed at page107, lines 14-20 of the specification and in Figure 26 and a skilled artisan would easily recognize start and stop codons and other signatures and homologies of the non-coding regions (see pages 17 of response). In response to this, whether theses features are disclosed does not lead to possession of polypeptides as broadly claimed where the specification does not disclose any polypeptides that are 80-99% identical to SEQ ID NO:69 or nucleic acids encoding such polypeptides. The response further states that the claims have been amended to encompass the characteristic that the nucleic acid encoding the polypeptide is amplified in lung and colon tumors and PRO357 is overexpressed in lung

and colon tumors. In response to this argument, while it is true that only SEQ ID NO:68 is amplified, the specification does not have written description for any polypeptide that is at least 80% to SEQ ID NO:69 wherein the nucleic acid encoding such is amplified in colon or lung tumors. The response further states that the analysis for determining whether the present specification provides written description my be performed by the methods in the revised Interim Written Description Guidelines Training Materials published at the PTO website (see page 19-20). The response states that Example 14 of the Guidelines is directed to a protein and variants thereof having 95% sequence identity, all of which have the same biological function and the claim satisfies the requirements of 112 fist (see page 20 of response). The response further states that analogous to Example 14 of the Guidelines, the present specification discloses and actually reduces to practice a polypeptide recited in claims 22-26, 33-34, (i.e. SEQ ISD NO:69) as well as a nucleic acid sequence encoding PRO 357 and moreover the polypeptide variants encompassed within claim 22-26, 33-34 do not have substantial variations with SEQ ID NO:69 because they have 80% to 99% identity to SEQ ID NO:69 or the nucleic acid encoding SEQ ISD NO:69. As such the nucleic acids of claims 22-26 and 33-34 all share the common structural features of 80-99% and common functional features of being encoded by a nucleic acid that is amplified in lung and colon tumors (see page 20 of response). In response to this argument, Example 14 of the Guidelines is directed to an enzyme that has the sequence of SEQ ID NO:3 or is 95% identical to SEQ ID NO:3 and catalyzes the reaction of A to B. The instant claims are directed to polypeptides that are 80-99% identical to SEQ ID NO:69 wherein the nucleic

acids are amplified in lung and colon tumors. While the claims require the amplification of the nucleic acid, this "function" is only the "function" of SEQ ID NO:68, the specification does not disclose any other polypeptides or how one would find a polypeptide that is 80-99% that would be encoded by a nucleic acid be that is amplified in lung or colon tumors. The specification teaches that the method to "assay" for expression requires the nucleic acid of the PRO nucleic acid of SEQ ID NO:68 or an antibody to the protein of SEQ ID NO:69 (see page 69). The specification does not teach how one would or could find any other polypeptide that is 80-99% to SEQ ID NO:69 which is encoded by a nucleic acid that is amplified in lung or colon tumors or which regions or parts of the nucleic acid of SEQ ID NO:68 would be used to find such. The specification does not provide written description for the claimed polypeptides.

11. The rejection of claims 22-36 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

The response filed 11/6/03 has been carefully considured but is deemed not to be persuasive. The response states that the claims have been amended that the polynucleotides are encoded by a nucleic acid that is amplified in lung and colon tumors and one skill in the art would recognize that the polypeptides encoded by PRO357 DNA which was determined to be amplified in Example 28 would function as diagnostic markers and Moreover, even if the PRO357 polypeptides did not follow the amplification

pattern of the nucleic acid encoding PRO357, the skilled artisan would recognize that such an expression pattern would function in more accurate classification and in addition Dr. Ashkenazi declares that if a gene is amplified but the corresponding product is not that expression pattern functions to alert a clinician that she should not employ a treatment utilizing agents that target the gene product (see page 23-24). In response to this argument, again the only nucleic acid that is amplified is SEQ ID NO:68 which encodes SEQ ID NO:69. there is no other nucleic acid other than SEQ ID NO:68 that is shown to be amplified. In addition, it would be undue experimentation to determine the myriad of polypeptides that are 80-99% to SEQ ID NO:69 which are encoded by nucleic acids that are amplified in lung and colon tumors. The specification does not teach how to use such polypeptides or how to find such. The declaration of Dr. Ashkenazi adds nothing with respect to enablement. The statement only states that if the protein is not expressed then one would not target the protein. There is no evidence that the polypeptide of SEQ ID NO:69 or any polypeptide that is 80-99% to SEQ ID NO:69 is amplified in lung or colon tumor. The response further states that the Examiner contends that the claims encompass an unreasonable number of inoperable polypeptides and cites references that single amino acid changes can have a dramatic and unpredictable effect on protein function and the response states that while this may be true one skill in the art would know that there are numerous nucleic acids, encoding non-conserved amino acids that could be changed in a sequence without substantially altering the structure, function, activity of the polypeptide (see page 24 of response). In response to this argument, the art sited by the examiner is evidence that alteration of a

polypeptide sequence is unpredictable and this is even more true as the PRO357 protein does not has a function or activity in order to determine if alterations in the amino acid sequence can be tolerated. The response further states that there are several methods for substituting amino acids in sequences and one can substitute conservative as well as non-conservative amino acids yet maintain the PRO357 function (see page 25 of response). In response to this argument, while one can alter the amino acid sequence of the PRO357 protein, again the art sited by the examiner is evidence that alteration of a polypeptide sequence is unpredictable and this is even more true as the PRO357 protein does not has a function or activity in order to determine if alterations in the amino acid sequence can be tolerated. The response further relies on the declaration of Dr. Ashkenazi which has been addressed above (see page 26). The response further cites Brodeur as evidence that gene amplification in cancer in which there is a very high correlation between gene amplification and protein over-expression (see page 26). In response to this argument, protein expression in cancer is not trivial and must be determined on a case by case basis. The specification does not demonstrate that the polypeptide of SEQ ID NO69 is overexpressed and in addition the prior art cited in the rejection demonstrates the unpredictability in the art which was not addressed in the response except for the Fu reference.

In view of the lack of guidance, lack of examples, and lack of predictability in the art as evidenced from the above references, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of

this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

LARRY R. HELMS, PH.D
PRIMARY EXAMINER